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BANNER & WITCOFF
1001 G STREET N W
SUITE 1100
WASHINGTON, DC 20001

EXAMINER
KAPUSHOC, STEPHEN THOMAS

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/715,117	LI ET AL.	
	Examiner	Art Unit	
	Stephen Kapushoc	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-3 are pending and examined on the merits.

This Office Action is in reply to Applicants' correspondence of 09/12/2006. Claims 4-134 are cancelled; no claims are withdrawn; no claims have been newly added; claim 1 has been amended. Applicants' remarks and amendments have been fully considered but are not found to be persuasive.

Any new grounds of rejection presented in this Office Action are necessitated by Applicants' amendments. Any rejections or objections not reiterated herein have been withdrawn.

This Action is made FINAL.

Priority

1. This instant application claims priority to provisional applications 60/427,202 (filed 11/19/2002) and 60/434,434 (filed 12-19-2002). However, the subject matter of the examined claims (claims 1-3, methods using SPHK1 gene copy number) was not disclosed in the '202 provisional application, thus the claims do not have priority to the '202 provisional application. The subject matter of the examined claims is disclosed in the '434 provisional application, thus the claims have priority to the 60/434,434 provisional application (filed 12-19-2002).

Claim Rejections - 35 USC § 112 1st - Enablement

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Nature of the invention and breadth of the claims

The claims of the instant application are drawn to methods for diagnosing cancer comprising determining copy number of an SPHK1 gene.

The rejected claims encompass analysis of any mammalian organism, including any non-human mammal.

The rejected claims encompass determining the copy number of any 'SPHK1 gene'.

The rejected claims encompass any level of gene amplification.

Claims 1 and 3 encompass comparison of a gene copy number to any control gene copy number.

Claims 1 and 2 encompass the diagnosis of any form of cancer.

The nature of the claims requires knowledge of a correlation between any level of amplification of any 'SPHK1 gene' and the presence of cancer.

Direction provided by the specification and working example

The specification of the instant application asserts that it has been determined that SPHK1 is amplified and/or overexpressed in human cancers (p.66). The specification asserts that human chromosome region 17q25 is one of the most frequently amplified regions in human cancer, and that in the process of characterizing a 17q25.2 amplicon SPHK1 was found amplified in several tumor samples (p.67). The specification teaches that amplification of SPHK1 was determined by microarray

analysis (p.67).

The specification teaches several definitions relevant to the breadth of the rejected claims. The specification teaches that 'cancer' includes the presence of cells possessing characteristics typical of cancer-causing cells, and specifically includes leukemic cells. The specification further defines a 'gene' as a region on genome capable of being transcribed to an RNA that has a regulatory or catalytic function or encodes a protein and encompasses spice variants, allelic variants, and transcripts arising from alternative promoter or poly-adenylation sites (p.33). The specification further defines SPHK1 as encompassing polymorphic variants, alleles, mutants, and interspecies homologs with various, not clearly defined, levels of homology and identity to GenBank NM_021972 (nucleic acid sequence), Genbank NP_069907.2 (polypeptide sequence), and SEQ ID NO: 1, 2, and 3 (nucleic acid and polypeptide sequences). (p.66).

Because the claimed method comprises determining gene amplification, it is relevant to point out that the instant specification broadly defines the term 'amplification' as encompassing amplification, duplication, and multiplication, of a gene yielding about 3.0 fold or more copies. However, an SPHK1 gene copy number of less than 3.0 fold can still be considered an amplification (p.34). The specification further defines an 'amplicon' as the amplification product of a gene, indicating that the term includes partially amplified SPHK1 (p.35).

Thus given the definitions provided by the specification, 'amplification of the SPHK1 gene' encompasses any amount of duplication of any portion of a gene

sequence with even a small degree of sequence similarity to the SPHK1 gene in any mammal. For example, a polymorphic variant of an SPHK1 pseudogene in a rabbit which contains a three nucleotide repeat insertion would be a gene amplification.

The specification provides an example of the analysis of SPHK1 gene amplification in cells from human tumors (Examples I, II, and III, pages 111-114). The Examples of the specification teach that DNA microarray based CGH was used to survey the genome for gene amplification, and it was determined that SPHK1 is frequently amplified in tumor tissues and cell lines. The specification teaches analysis of SPHK1 gene copy number in breast, ovarian, colon, bladder, and lung tumors (Table 1). The specification teaches that SPHK1 gene amplification was detected from 3% to 33% of the time. For example, amplification was detected in 1 out of 30 lung tumor samples; it is not established by the specification if such results indicate that SPHK1 amplification can be used to reliably diagnose lung cancer. Even in the case of bladder cancer, where amplification was found in 3 out of 9 samples (33%), it is not determined that such a result with a sample size of 9 (n=9) indicates a statistically significant correlation between gene amplification and cancer.

The specification does not teach what level of amplification (i.e. –fold amplification) was found in any of the samples for which data is included in Table 1. The specification teaches that while amplification of less than 3.0-fold can still be considered as an amplification, only samples with the SPHK1 gene copy number greater than or equal to 3.0-fold are deemed to have been amplified because of detection limits (p.111). Thus the claims encompasses methods (determining any level

of amplification) which were not able to be analyzed by the methods of the instant application. However, Table 2 appears to indicate amplification levels lower than 3.0-fold. It is not clear from the instant specification what is meant by a fractional fold of amplification (for example, 1.6 fold for MDAMB134 in Table 2). Does this indicate that only a portion of the gene was amplified? Similarly, Table 2 includes a measure of 0.8-fold amplification; does this represent a loss of a gene or portion of the gene.

Furthermore, the reporting of '-fold amplification' is not clear within the specification (p.34), as the specification does not clearly set forth what is considered a '-fold amplification'. For example, assuming that a non-cancer sample has two copies of a gene (diploid), would detection of three copies of the gene in a tumor sample be considered a 1.5-fold amplification (2 x 1.5 = 3), or considered a 1-fold amplification (there is 1 more copy of the gene), or considered a 3-fold amplification (there are 3 copies of the gene), or some other -fold amplification. Is fold amplification reported relative to a non-cancer sample, or an absolute number of copies of the gene in a sample.

The instant specification does not provide any measure of the statistical significance of the reliability with which SPHK1 gene amplification can be used to diagnose cancer.

The instant specification provides no analysis of SPHK1 gene amplification or cancer diagnosis in any non-human mammals.

The specification does not teach the relationship between the genomes surveyed to determine gene amplification (p.111) and the tumor genomes analyzed for the data in

Table 1, thus it is not known if the method was validated in an external population.

The specification does not provide the sequence of the microarray probes used to determined SPHK1 gene amplification, nor the method in which gene amplification was determined for the data in Table 1, nor the nature of the amplicon (e.g. the portion of the SPHK1 gene that is amplified in a tumor sample).

State of the art, level of skill in the art, and level of unpredictability

While the state of the art and level of skill in the art with regard to the detection and quantitation of a particular nucleic acid sequence in a sample is high, the level of unpredictability in associating any particular gene or copy number of a gene with a phenotype is even higher. The level of unpredictability is demonstrated by the prior art, the post filing art, and the instant specification.

Though the prior art teaches a role of sphingosine kinase in the development of cancer phenotypes (Xia et al, 2000, as cited in the IDS), the prior art does not teach the reliable association of SPHK1 gene amplification with the diagnosis of cancer in mammals. The unpredictability in using determination of SPHK1 gene amplification for cancer diagnosis is demonstrated by the prior art. For example, Teixeira et al (1998) teaches that in a case of male breast cancer there was noted a loss of chromosome 17 (monosomy 17) (p.19, left col., lns.1-3; Fig.1). Similarly, El-Naggar et al (1999) teaches the loss of chromosome 17 in breast, kidney, and lung tumor cells (Table 2; p.110, right col., lns.14-16. It is thus unpredictable as to whether or not amplification of SPHK1 (located on chromosome 17) would be detected in these tumors in which chromosome 17 has been lost. Additionally, as claims 1 and 2 are drawn to diagnosis of all cancers

(and the specification specifically recites leukemic cells as a cancer (p.30)), it is relevant to point out the post filing art of Mo et al (2006). Mo et al teaches a translocation that is causative of acute monoblastic leukemia: t(8;18;16)(p11;q21;p13) (Fig 1). It is unpredictable as to whether or not analysis of SPHK1 gene amplification (located on chromosome 17) would allow for the diagnosis of this cancer in which t(8;18;16)(p11;q21;p13) is the sole chromosome aberration (p.75 - Introduction).

While the specification does not provide any statistical analysis of the data presented in Tables 1 and 2, the prior art of Thisted (1998) indicates the requirements necessary to establish statistical significance. Thisted teaches that it has become scientific convention to say that associations are considered statistically significant when p-values (the p-value being a measure of how much evidence exists against a null hypotheses, a null hypothesis typically being that there is no causal association between tested variable and the results, with a larger p-value providing less evidence against the null hypothesis) are less than or equal to 0.05 (p.5). Additionally, post-filing art reveals that most gene association studies are typically wrong. Lucentini (2004) teaches that it is strikingly common for follow-up studies to find gene-disease associations wrong (left column, 3rd paragraph). Lucentini teaches that two recent studies found that typically when a finding is first published linking a given gene to a disease there is only roughly a one-third chance that the study will reliably confirm the finding (left column, 3rd paragraph). Lucentini teaches that bigger sample sizes and more family-based studies, along with revising statistical methods, should be included in the gene association studies (middle column, 1st complete paragraph). It is thus not

established by the teachings provided in the instant specification whether or not a measure of SPHK1 gene copy number is a reliably indicator of cancer.

And while the specification teaches the breadth of the term 'SPHK1 gene', the examples presented in the specification do not address the different sequences encompassed by the claims. For example while the claims encompass analysis of any polymorphic variant, the specification does not teach the analysis of any variants of the SPHK1 gene. The art teaches a variety of polymorphisms in the SPHK1 gene including at least 27 SNPs (GeneCard for protein-coding SPHK1, pages 7-8). Notably, one SNP (rs3744040; CAG to TAG) creates a Gln to STOP codon change in the protein-coding region. Based on the prior art of Xia et al (which teaches a role of over expression of the sphingosine kinase in cancer development) coupled with the teachings of the instant application (which asserts that gene amplification leads to overexpression (Table 2)), it is unpredictable as to whether or not amplification of a gene containing, for example, the rs3744040 SNP (coding for a truncated amino acid sequence), or any other SNP, would be indicative of cancer.

Because the claims encompass the analysis of a sample from any mammal, it is relevant to point out the unpredictability in using a human nucleic acid sequence in the analysis of a sample from any other organism. While it is generally held true that structure correlates with function, Bork et al (1993) teaches an analysis of sugar kinases, and indicates that very distinct proteins (with different three-dimensional structures and strikingly different sequence patterns) can catalyze chemically equivalent reactions of similar or identical substrates (p.31 - Abstract). Thus a sphingosine kinase

gene associated cancer in a non-human mammal may be quite dissimilar to the human gene sequence as set forth in SEQ ID NO: 1. Similarly, the converse line of reasoning demonstrates that just finding a gene comprising a sequence similar to SEQ ID NO: 1 or encoding a protein with an amino acid sequence similar to SEQ ID NO: 3 in any non-human mammal does not necessarily mean that amplification of the gene will be indicative of a cancer diagnosis. It is possible that an apparent homolog (i.e. a gene with a high percentage of sequence homology) might not be functionally equivalent to the human SPHK1 gene disclosed in the instant application (SEQ ID NO: 1, 2, and 3). Such a possibility is exemplified by Juppner (1995), which teaches that despite significant structural conservation, rat, opossum, and human PTH/PTHrP receptor homologs display distinct functional characteristics (Abstract; pp.39S-40S). Thus, analysis in a non-human mammal of gene amplification of any gene similar to the human SPHK1 gene analyzed in the examples of the instant application would require experimentation to determine whether or not amplification of the genes would be useful in diagnosing cancer.

Quantity of experimentation required

A large amount of experimentation would have to be performed in order to make and use the claimed invention. Such experimentation would include examining any possible variant of the SPHK1 gene from any mammal to establish a statistically significant association between any level of gene amplification and any form of cancer. Even the application of the method to specifically recited forms of cancer would require validation of the method in case:control studies as well as the validation of the method

using every possible gene variant in other non-human mammals. Such experimentation would involve the analysis of an enormous number of nucleic acid sequences, and large case:control studies in multiple human populations as well as non-human populations.

Conclusion

Taking into consideration the factors outlined above, including the nature of the invention and breadth of the claims, the state of the art, the level of skill in the art and its high level of unpredictability, the lack of guidance by the applicant and the lack of working examples, it is the conclusion that an undue amount of experimentation would be required to make and use the claimed invention.

Response to Remarks

Applicant has not traversed the rejection of claims under 35 USC 112 1st¶ as lacking enablement.

This rejection is MAINTAINED.

Claim Rejections - 35 USC § 112 1st – Written Description

4. Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is referred to the revised interim guidelines on written description published January 5, 2001 in the Federal Register, Volume 66, Number 5,

page 1099-111 (also available at www.uspto.gov).

The rejected claims are broadly drawn to methods for diagnosing cancer comprising determining SPHK1 gene copy number. The rejected claims provide no structural limitation regarding what is encompassed by the term 'SPHK1 gene'.

When the claims are analyzed in light of the specification, the instant invention encompasses methods comprising the analysis of an enormous and wide variety of nucleic acid sequences. The claims are broadly drawn diagnosing cancer by determinig SPHK1 gene copy number in a test sample. The specification teaches a broad definition of 'gene' as a region on the genome that is capable of being transcribed to an RNA (p.32), and encompasses all SPHK1 transcripts that may be found including splice variants, allelic variants, and transcripts that occur because of alternative promoter sites or alternative poly-adenylation sites (p.33). The specification further teaches a broad definition of 'SPHK1', indicating that the term SPHK1 may include polymorphic variants, alleles, mutants, and interspecies homologs that have (i) for example as little as 60% nucleotide identity to GenBank NM_021972, (ii) as little as 65% amino acid homology to GenBank NP_068807.2, (iii) for example as little as 60% homology with the nucleotide sequence of SEQ ID NO: 1, or (iv) 'substantial sequence homology with the encoded amino acid (for example, SEQ ID NO: 2)' with no clear definition of 'substantial sequence homology' (p.66). The specification further teaches that 'SPHK1 polynucleotides' typically come from any mammal (p.66). Additionally, the specification teaches a definition of 'amplicon' as an amplification product that may include a part of SPHK1 (p.35). Thus the rejected claims encompass analysis of any portion of any

variant of any SPHK1 gene from any organism, which may include gene sequences very different from the disclosed SEQ ID NO: 1, and genes that encode polypeptides very different from the disclosed SEQ ID NO: 2, including sequences containing any polymorphisms (e.g. any insertion, deletion, or repeat at any location within the gene) and mutations not taught by the instant specification and not yet known in the art. In analyzing whether the written description requirement is met for genus claims for genus claims, it is first determined whether a representative number of species have been described by their complete structure. Nucleic acids of such a large genus as encompassed by the rejected claims have not been taught by the specification. The specification of the instant application discloses only SEQ ID NO: 1 (a human SPHK1 DNA sequence), SEQ ID NO: 3 (the protein coding portion of SEQ ID NO: 1), and SEQ ID NO: 2 (the amino acid sequence encoded by SEQ ID NO: 3).

Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (i.e. other than nucleotide sequence, gene name, and specific polymorphic position), specific features and functional attributes that would distinguish different members of the claimed genus. In the instant case, the specification provides only the sequence of the human SPHK1 gene (SEQ ID NO: 1 and 3) and the encoded amino acid sequence (SEQ ID NO: 2). The specification does not provide any characteristics that would allow one to identify any other genes from another organism or any particular portions or fragments or

variants of the disclosed sequence that would allow for the diagnosis of cancer based on amplification of the non-disclosed gene.

> Applicants' attention is directed to the decision in *In re Shokal*, 113 USPQ 283 (CCPA 1957) wherein is stated:
>
> > It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. In re Soll, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189; In re Wahlforss et al., 28 C.C.P.A. (Patents) 867, 117 F.2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary.

In the instant application, with the exception of a method for diagnosing cancer comprising determining the copy number of a gene consisting of the particular sequences disclosed in the specification, one of skill in the art cannot envision the detailed chemical structure of the encompassed polynucleotides (i.e. any SPHK1 genes the amplification of which is indicative of cancer), regardless of the complexity or simplicity of the method of identification. Adequate written description requires more than a mere statement that any genetic variants or fragment of the gene is part of the claimed invention and a qualitative description of the nature of the variant (e.g. amplification is associated with cancer). The nucleic acid itself is required.

In conclusion, the limited information provided regarding the association of SPHK1 (including disclosure only of SEQ ID NO: 1, 2, and 3) gene amplification with cancer is not deemed sufficient to reasonably convey to one skilled in the art that

Applicant is in possession of methods comprising the analysis of any gene variants or fragments besides those particularly disclosed in the specification at the time the application was filed.

Thus, having considered the breadth of the claims and the provisions of the specification, it is concluded that the specification does not provide adequate written description for the claims.

Response to Remarks

Applicant has traversed the rejection of claims under 35 USC 112 1st¶ for lack of written description arguing that the naturally occurring SPHK1 gene is well known in the art. This argument has been fully and carefully considered but is not found to be persuasive. As detailed in the rejection, the definition of 'SPHK1' gene as provided in the instant specification (pages 33 and 66 of the instant specification) considerable broadens what is encompassed by the claimed method comprising 'determining sphingosine kinase 1 (SPHK1) gene copy number'. Thus the claims encompass determining gene copy number of genes with nucleotide sequences well beyond what might be considered 'the naturally occurring SPHK1 gene'. And while applicant cites *Capon v Eshhar* to indicate that the specification does not require a nucleotide sequence when 'that sequence is already known in the art', in the case of the instant application the examiner maintains that the claims are drawn to an enormous variety of nucleic acid sequences, as indicated on page 66 of the specification, and neither the instant specification nor the teachings of the art, in fact teach methods for diagnosing

cancer in any mammal using any of the sequences encompassed by the claims.

The rejection is MAINTAINED.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Suehiro et al (2000).

Suehiro et al teaches the comparative genomic hybridization analysis of ovarian carcinoma cells.

Regarding claim 1, the reference teaches CGH analysis of DNA extracted from trimmed tumor samples (p.51 – CGH). The reference specifically teaches the analysis of copy number of the chromosomal region 17q25-qter, a region which encompasses the human SPHK1 gene. Thus the analysis of tumor DNA by CGH is determining SPHK1 gene copy number in a sample from a region suspected to be cancerous and generating data for a test gene copy number (p.51 – Microscopy and digital image analysis), relevant to part (a) of claim 1. Relevant to part (b), the reference also teaches the CGH analysis of normal DNA (p.51 –CGH), and the simultaneous analysis of labeled DNA (from tumor and normal tissue) by hybridization to normal metaphase spreads. Thus the analysis results in a comparison of test and control gene copy

numbers. The reference further teaches that amplification of the 17q25-qter region (which contains the SPHK1 gene) indicates the presence of cancer (p.53 correlations between clinical stages and CNAs; Table 4; Table 5).

Regarding claim 2, the reference teaches the use of normal DNA as a control, and hybridization to normal metaphase spreads (p.51 – CGH). Thus the comparison to the control is a comparison to a normal diploid sample in which the copy number of the 17q25-qter region is two copies per cell.

Regarding claim 3, the reference teaches the analysis of ovarian clear cell carcinomas (p.51 – Tumor material), which is the analysis of an ovarian cancer.

Response to Remarks

Applicant has traversed the rejection of claims under 35 USC 102 as anticipated by Suehiro et al. Applicant argues that Suehiro et al does not expressly or inherently teach determining SPHK1 gene copy number or that amplification of an SPHK1 gene in a test sample relative to a control indicates the presence of a precancerous lesion or cancer in a mammal. This argument has been fully and carefully considered but is not found to be persuasive.

The Examiner maintains that the CGH analysis of Suehiro et al, with particular attention to the amplification of 17q25-ter, is an analysis of SPHK1 because the SPHK1 gene is included in this genomic region (see also for example instant specification p.27 lns.11-12). Additionally, the Examiner maintains that Suehiro et al does teach analysis of gene copy number (p.51, right col., last line – p.52, left col., line 9), where

amplification from a tumor sample is compared to copy number from blood lymphocytes (p.51 – CGH). Furthermore, Suehiro does teach a significant correlation between 17q25-ter CNA (copy number abnormality) and ovarian cancer (Tables 4 and 5), indicating that the 17q25-ter amplification is the presence of cancer.

The rejection is MAINTAINED

Conclusion

No claim is allowable. No claim is free of the prior art.

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Kapushoc whose telephone number is 571-272-3312. The examiner can normally be reached on Monday through Friday, from 8am until 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen Kapushoc
Art Unit 1634

Carla Myers
CARLA J. MYERS
PRIMARY EXAMINER